REMARKS

Claims 1-34 are pending. Claims 7 and 8 have been canceled. Claims 9-13 and 18-34 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 3, 4, and 16 have been amended to more clearly claim what Applicants consider to be their invention.

Claim 1 was amended to recite wherein the polypeptide is capable of forming an amphipathic helical structure. Support for amended claim 1 can be found at least on page 45, line 22-page 48, line 9 where the determination that the polypeptides of the invention form an amphipathic α helical structure is described.

Claim 3 as amended to recite the polypeptide of claim 1, wherein the polypeptide comprises from 14 amino acids to 18 amino acids in length. Support for claim 3 can be found at least in original claim 1, where the polypeptides of the invention are described as well as in SEQ ID. NOs: 1-207.

Claim 4 was amended to remove sequences to non-elected inventions. Support for claim 4 can be found at least in original claim 4. Applicants also note that as each of the species previously listed in claims 4 and 5 properly fall within the elected genus, Applicants therefore remind the Examiner that if the elected genus is found to be allowable, all of the species previously listed in claims 4 and 5 should also be found allowable.

Claim 16 was amended to correct a grammatical error. Support for claim 16 can be found at least in original claim 16.

CLAIM OBJECTIONS

Claim 4 was objected to for reciting multiple sequence identifiers which refer to identical sequences. Claim 4 was also objected to for reciting non-elected subject matter. Claim 4 has been amended to refer only to SEQ ID NO:5. As such, Applicants respectfully request that the objection be removed.

Claim 7 was objected as allegedly being of improper dependent form for failing to limit the subject matter of a previous claim. Claim 7 has been cancelled. As such, Applicants respectfully submit that the objection is made moot.

Claim 16 was objected to for reciting a grammatical error. Claim 16 has been amended to correct the grammatical error. As such, Applicants respectfully request that the objection be removed.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-4, 6-8, and 14-17 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Any analysis of whether a particular claim is enabled by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 8

USPQ2d 1217 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343, 199 USPQ 659 (CCPA 1976). A patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987). Determining enablement is a question of law based on underlying factual findings. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984).

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *M.I.T. v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt,* 537 F.2d 498, 190 USPQ 214 (CCPA 1976).

The Office Action on page 4, lines 15-17, alleges that claims 1-4, 6-8, and 14-17, while being enabled for the polypeptide comprising SEQ ID NO:5, does not provide enablement for the broad genus of polypeptides as claimed. The Examiner appears to base the rejection on two different bases which will be addressed individually.

First, the Examiner appears to base his rejection on the notion that the polypeptide recited in claim 1 is broad and allows for a number of permutations within the core sequence. The Examiner goes on to reference "the art" to support theories that substitution of amino acid residues is complex and the effects on protein function are not easily predicted, in fact, the Examiner states that the "unpredicatable effects" of changes to the amino acids on protein shape and function would require undue experimentation to determine how to use the genus of compounds recited in claim 1. (See Office Action page 5, lines 7-9). The Examiner goes on to

cite Weers et al. and Zaiou et al. to illustrate the structure and function of the apolipoprotein E molecule are tied to one another, such that changes in the primary structure of the apolipoprotein E molecule can change the function of the molecule.

Applicants first note that claim 1 has been amended to recite "wherein the polypeptide is capable of forming an amphipathic α helical structure". As such, the polypeptides recited in claim 1 have a finite structure. While it is true that claim 1 allows for a number of permutations within the core sequence, the number of permutations is not only limited by the number of possible permutations, but the amino acid substitutions are restricted to the specific locations and amino acid residues that can be substituted. Furthermore, no matter how many permutations are possible, each and every polypeptide within the genus is capable of forming the same structure, namely an amphipathic α helical structure. This ability stems from the fact that the amino acids that can be substituted in the core sequence and the locations in which the specific amino acids can be inserted, has been thoroughly calculated and analyzed such that each and every polypeptide encompassed by claim 1 is capable of forming an amphipathic α helical structure. Example 1 also describes computer programs used to identify and classify amphipathic α helical domains of polypeptides. It is the amphipathic helical structure that contains at least one Arg residue on the polar face of the amphipathic helix that allows the claimed polypeptides to associate with atherogenic LDL and VLDL and remnant lipoproteins to enhance their hepatic uptake and degradation. (See Example 1). As such, the skilled artisan would not have to resort to a large degree of experimentation to determine how to use the claimed polypeptides as the

specification establishes the function and further provides a road map of how the experiments were performed such that one of skill in the art could easily follow.

Second, the Office Action provides that only claims 14 and 15 recite any function and therefore claim 1 encompasses proteins which neither enhance binding to, nor enhance degredation of, LDL or VLDL. (See Office Action page 5, lines 15-18). The Office Action further states that the specification does not teach how to use proteins which do not enhance degredation of LDL or VLDL and further alleges that there is no evidence that the generic structure of SEQ ID NO:210 imparts any particular function common to all members of the genus. Applicants are unaware of any requirements that each embodiment of an independent claim must have the same or a common function in order to be enabled. In fact, Applicants submit that no such requirement exists. Applicants also note that claims 14 and 15 are dependent claims. As such, they are by definition narrower than the claim from which they depend, namely claim 1. Therefore, each of the recited polypeptides are not required to have the function of claims 14 and 15. Even if it were true that some of the recited polypeptides neither enhance binding to, nor enhance degredation of, LDL or VLDL, the specification provides other functions which the claimed polypeptides of claim 1 have. Specifically, the specification provides on page 37, lines 14-18 "the polypeptides or peptides of the invention may also be used to generate antibodies, which bind specifically to the polypeptides or fragments of the polypeptides. The resulting antibodies may be used in immunoaffinity chromatography procedures to isolate or purify the polypeptide or to determine whether the polypeptide is present in a biological sample." Therefore, particular functions such as the ability to enhance binding to, or enhance degredation of, LDL or VLDL, as well as the ability to produce antibodies are fully described.

Therefore, Applicants respectfully submit that the specification not only teaches how to use the polypeptides recited in claim 1, but the specification provides how to use the claimed polypeptides. Applicants further submit that due to the extensive teachings cited above, it would not require undue experimentation on the part of a skilled artisan to make and use the claimed invention commensurate in scope to the claims. For at least these reasons, Applicants submit that claims 1-4, 6-8, and 14-17 are fully enabled. As such, Applicants respectfully request withdrawal of this rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-8 and 14-17 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

The Office Action states that the specification provides adequate written description for the isolated nucleic acid sequences designated as SEQ ID NOs:1-207. (See Office Action page 6, lines 2-5). However, the Office Action alleges that the specification fails to indicate that the Applicants were in possession of every embodiment of polypeptides that could fall within the scope of SEQ ID NO:210. (See Office Action page 6, lines 5-7). By this logic, the Examiner appears to be applying *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) in a way that would require as the possession standard that the actual sequence of each and every embodiment of the polypeptides that fall within the scope of claim 1 must be specifically recited to meet the written description standard. Applicants submit that this is simply not the law.

Applicants note that the mere absence of some specific description in a specification of some embodiment or aspect of a claimed invention does not, by itself, constitute a lack of adequate written description. Rather, the test is that the applicant conveys with reasonable clarity to those of skill in the art that he or she invented what is claimed. *Vas-Cath v. Mahurkar,* 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). It is clear that every detail of every embodiment is not required. In fact, the Office Action on page 6, lines 17-19, refers to *Regents of the University of California v. Eli Lilly & Co.,* 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) which held that a genus claim may be supported by a representative number of species, not the full gamut of species. Of importance is the portion of *Lilly* which states an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." citing *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997).

Furthermore, it has been repeated over and over by the Federal Circuit that "the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo Biochem vs. Gen-Probe Incorporated,* 296 F.3d 1316, 1324, 63 U.S.P.Q.2d 1609 citing the Written Description Guidelines, 66 Fed. Reg. at 1106. This standard, as well as many others is viewed through the eyes of the skilled artisan. As discussed below, there can be no doubt that claims 1-8 and 14-17 meet this standard.

Lilly, 119 F.3d at 1567 held that a method of obtaining an unknown gene was not adequate written description for the gene itself when nothing was known about the structure of the gene itself. This is not the case here. In fact, the structure of the claimed polypeptides is explicitly recited in claim 1, namely claim 1 recites the amino acid sequence of the claimed polypeptide and that the polypeptide is capable of forming an amphipathic α helical structure. The fact that the structure of the claimed polypeptides is specifically provided, differentiates the current claims from the holding in *Lilly* and satisfies the standard of *Enzo*. In addition, as recognized in the Office Action, Applicants have provided 52 examples of species that fall within the scope of currently amended claim 1. Not only have applicants named the species, but Applicants have provided the specific sequences of the species and as described above, the specific structure of each of the species. In summary, Applicants have provided the sequence of the genus, the structure of the genus, and 52 examples of species that fall within the genus along with there specific sequence and structures. At least for these reasons, Applicants submit that such a disclosure satisfies the holdings of *Lilly* and *Enzo* and therefore satisfy the requirements of 35 U.S.C. 112, first paragraph.

Contrary to position of the Office Action with respect to *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), *Amgen Inc. v Chugai Pharaceuticals Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991) and *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, reduction to practice of each member of a genus is not required. Furthermore, *Fiers, Amgen, and Fiddes*, all support the state of the law as set forth in *Lilly* and *Enzo*, for example, that some structure with a means to identify the function of members of the genus is sufficient to describe a genus of compounds that are both structurally and functionally related, such as the structure set forth in claim 1.

Furthermore, as discussed above, in the present application, these cases can also be distinguished in that the structure of the composition being claimed is provided both in the claims and in the specification, and in *Fiers* and *Lilly*, the structure of the composition being claimed was unknown.

The rejections also fail to establish how it is that a lack of specific description of more embodiments of the claimed polypeptides could constitute a lack of adequate written description. The rejections, although lengthy, consist almost entirely of statements regarding what is encompassed by the claims, what is specifically described in the specification, comparison of what is claimed and what is described in the specification, and conclusions (that are supported only by the statements and comparison) that the specification lacks adequate written description. With respect, more than this is required. The rejections must provide reasons why those of skill in the art would find the written description inadequate; that is, why they would not recognize that Applicants invented what is claimed. Reference in the specification to known materials, even in the absence of more specific description of numerous embodiments of such materials, would not constitute a lack of adequate written description because those of skill in the art would not miscomprehend that nature and use of such known materials. Because the present rejections fail to support the conclusions drawn in the present rejections, the rejections fail to establish a prima facie case of lack of adequate written description. For this additional reason, Applicants submit that the current disclosure satisfies the requirements of 35 U.S.C. §112, first paragraph.

In addition, Claim 8 was rejected on the basis that Applicants allegedly did not provide evidence that they were in possession of any peptidomimetics. Claim 8 has been cancelled. As such, Applicants respectfully submit that the rejection of claim 8 is made moot.

For all the reasons set forth above, Applicant submit that claims 1-8 and 14-17 are adequately described in the specification and comply with the requirements of 35 U.S.C. §112. As such, Applicants respectfully request the withdrawal of the rejection, and allowance of claims 1-8 and 14-17.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-8, 14-17 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the application regards as the invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

A. Claim 1 was considered indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that claim 1 is indefinite because the unamended claim 1 recited "consists of" after broad recitations using the term "comprising". In response, Applicants have amended claim 1 to recite "wherein the polypeptide is capable of forming an amphipathic α helical structure" and have removed the claim language "wherein the polypeptide consists of a single domain". Applicants submit that amended claim 1 is clear and definite.

The Office Action based the rejection on the notion that a broad range or limitation together with a narrow range or limitation that falls within the broad range f limitation (in the same claim) is considered indefinite. Applicants note that merely using narrowing language after a broad limitation in the same claim does not per se render a claim invalid, however, such an argument need not be developed in this case as the claim language the Office Action alleged

rendered the claim indefinite has been removed to more clearly claim what the Applicants consider to be their invention. As such, Applicants respectfully submit that the rejection is made moot.

B. Claim 1 was considered indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that claim 1 is indefinite because the unamended claim 1 recited the term "domain" which the Office Action alleged is a variable term. Applicants have amended claim 1 to recite "wherein the polypeptide is capable of forming an amphipathic α helical structure" and have removed the claim language "wherein the polypeptide consists of a single domain". Applicants submit that amended claim 1 is clear and definite.

C. Claim 3 was considered indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that claim 1 is indefinite because the unamended claim 3 recited "wherein the polypeptide comprises about 10 to about 30" which the Office Action alleged made it impossible to determine the metes and bounds of the claim. Applicants have amended claim 3 to recite "wherein the polypeptide comprises 14 amino acids to 18 amino acids in length" and have removed the claim language "about 10 to about 30". Applicants submit that amended claim 3 is clear and definite.

REJECTION UNDER 35 U.S.C. § 102

Claims 1-4, 6-8 and 14-17 were rejected under 35 U.S.C. § 102(b), as being anticipated by Harris et al. (U.S. Patent No. 5,87,153). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Harris et al. discloses heparin antagonist peptides that specifically neutralize heparin's conventional anticoagulant properties. The heparin antagonist peptides of Harris et al. are explicitly described in SEQ ID NOS: 1-11. (See Harris et al. columns 23-28).

The passages of Harris et al. cited in the Office Action fail to disclose a synthetic apolipoprotein-E mimicking polypeptide comprising an amino acid sequence X-Y-Arg-Arg-Y-Y-X-X-Y-Y-Arg-Y-Y-Arg (SEQ ID NO: 210), wherein X is glycine, threonine, serine or alanine, wherein Y is a hydrophobic amino acid. The passages of Harris et al. cited in the Office Action fail to disclose a synthetic apolipoprotein-E mimicking polypeptide comprising an amino acid sequence described above, wherein the polypeptide is capable of forming an amphipathic α helical structure.

Claim 1 and claims 2-4, 6-8 and 14-17 that depend from Claim 1, are drawn to a specific genus of polypeptides that are capable of forming a specific structure. Specifically, the claims are drawn to synthetic apolipoprotein-E mimicking polypeptides comprising an amino acid sequence X-Y-Arg-Arg-Y-Y-X-X-Y-Y-Arg-Y-Y-Arg (SEQ ID NO: 210), wherein X is glycine, threonine, serine or alanine, wherein Y is a hydrophobic amino acid, wherein the polypeptide comprises an acetyl group at the N-terminus and an amide group at the C-terminus, and wherein the polypeptide is capable of forming an amphipathic α helical structure. As such, the claims require that the polypeptide have a specific sequence (X-Y-Arg-Arg-Y-Y-X-X-Y-Y-Arg-Y-Y-Arg (SEQ ID NO: 210)) where each of the amino acids labeled as "X" or "Y" be a selected from a select set of amino acid residues. Each "X" and "Y" thus must each be in a specific positional relationship to the arginine backbone.

The Office Action alleges (page 8, lines 27-28) that claim 1 does not require the full-length sequence set forth as SEQ ID NO: 210, but rather only require "an amino acid sequence". The Office Action (page 8, lines 27-28) improperly parlays this into allegedly meaning that the claim is sufficiently broad to encompass fragments of the sequence as small as two amino acids. The Office Action then alleges that Harris et al. teaches SEQ ID NO:10, which comprises arginines at specific residue positions that correspond to the arginine residues of Applicants claimed SEQ ID NO:1. (See Office Action page 8, lines 29-31) In other words, the Office Action alleges that the fact that Harris et al. discloses an amino acid sequence that has arginine residues spaced out in positions similar to the sequence in claim 1, without taking into consideration the claim limitation that other amino acids must also be in specific positions relative to the arginines, anticipates claim 1. This is simply incorrect.

First, Applicants take issue with the Office Actions interpretation of claim 1. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App.

1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Claim 1 claims a specific genus of polypeptides that comprise specific sequences that are capable of forming a specific structure. The claim language "a synthetic apolipoprotein-E mimicking polypeptide comprising an amino acid sequence" followed by recitation of a specific sequence is to be properly interpreted as comprising the entire sequence with the possible inclusion of unrecited elements, not to comprise a subsection of the elements recited after such language. Applicants are unaware, and the Office Action has failed to direct the Applicants attention to, any case law that holds that use of the term "comprising" followed by recitation of a specific element can reasonably interpreted to encompass less than what is explicitly recited. Here, claim 1 explicitly recites a sequence and provides the particular amino acids that can be substituted at each of the specific positions in the generic polypeptide sequence. Applicants submit that the Office Action has mistakenly construed the claim too broadly.

Secondly, Applicants submit that Harris et al. fails to disclose a synthetic apolipoprotein-E mimicking polypeptide comprising an amino acid sequence X-Y-Arg-Arg-Y-Y-X-X-Y-Y-Arg-Y-Y-Arg (SEQ ID NO: 210), wherein X is glycine, threonine, serine or alanine, wherein Y is a hydrophobic amino acid. The Office Action cites Harris et al. SEQ ID NO:10 as allegedly teaching claimed sequence SEQ ID NO:210. Harris et al. SEQ ID NO:10 is not the same as the polypeptide of claim 1. The Office Action relies on the fact that Harris et al. SEQ ID NO:10 has arginine residues at positions 5, 6, 13, and 16 to support the allegation that Harris et al. SEQ ID NO:10 teaches claimed SEQ ID NO:210. What the Office Action fails to appreciate is the fact

that there is an addition arginine residue at position 9, which does not follow the sequence encompassed by the polypeptide of claim 1 as discussed above.

Applicants also note that Claim 1 recites a specific genus of polypeptides that comprise specific amino acids in specific positions. For example, the polypeptide of claim 1 comprises at least 7 hydrophobic amino acids in specific locations relative to the argnine residues of SEQ ID NO:210. SEQ ID NO:10 of Harris et al. does not comprise any hydrophobic amino acids, much less teach hydrophobic amino acids in specific positions relative to the arginine residues. This is not the same as the claimed polypeptide recited in claim 1. Nowhere in Harris et al. is a polypeptide comprising the specific sequence recited in claim 1 disclosed.

The cited passage of Harris et al. fails to disclose a synthetic apolipoprotein-E mimicking polypeptide comprising an amino acid sequence X-Y-Arg-Arg-Y-Y-X-X-Y-Y-Arg-Y-Y-Arg (SEQ ID NO: 210), wherein X is glycine, threonine, serine or alanine, wherein Y is a hydrophobic amino acid. Because Harris et al. fails to disclose every feature of the claimed polypeptides, Harris et al. fails to anticipate claims 1-4, 6-8 and 14-17. As such, Applicant respectfully request withdrawal of the rejection.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $510.00, $510.00 representing the fee for a small entity under 37 C.F.R. § 1.17(a)(3), and a Request for Three Month Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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